

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

**Lapatinib for breast cancer
(First line use in advanced or metastatic hormone-sensitive breast cancer)**

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of lapatinib in combination with letrozole in the first-line treatment of advanced or metastatic hormone-sensitive breast cancer

Background

Breast cancer is the most common cancer affecting women in the UK, accounting for nearly 1 in 3 of all cancers in women. In England and Wales, over 37,000 new cases were diagnosed in 2002, and there were over 11,000 deaths due to breast cancer in 2003.

There are many risk factors that predispose women to developing breast cancer, the strongest being increasing age. 80% of breast cancer occurs in post menopausal women (assuming average age of menopause is 50). Other risk factors include previous breast cancer, family history, early menarche, late menopause, number of children and genetic mutations.

Many breast cancers are stimulated to grow and change by naturally occurring female sex hormones, oestrogen and progesterone. Tumours that have receptors to these hormones are more likely to respond to hormonal therapies (drugs or treatments that block the effects of hormones, or lower the levels of oestrogen and progesterone), and patients with such tumours tend to have a better prognosis.

Advanced and metastatic breast cancer are defined by staging based on the tumour, node and metastasis staging system, falling within stages III and IV. Stage III denotes disease that is locally advanced and/or has spread to regional lymph nodes and stage IV denotes that distant metastasis has occurred. Between 16% and 20% of women presenting with breast cancer have advanced disease with distant metastases (5,750 to 7,200 women), and around 50% of those presenting with early or localised breast cancer will eventually develop metastatic breast cancer.

Tumours which over-express a receptor known as human epidermal growth factor receptor 2 (HER2, synonymous with ErbB2) are associated with poor prognosis and reduced overall survival. The average survival after diagnosis of metastatic breast cancer is 18-24 months. This is reduced by up to 50% for patients with tumours over-expressing HER2. Approximately 15% to 20% of

women with metastatic breast cancer have tumours which over-express HER2 at the 3+ level measured by an immunohistochemical technique¹.

The technology

Lapatinib (Tykerb, GlaxoSmithKline), is an oral therapy which inhibits the tyrosine kinase components of the ErbB2 (synonymous with HER2) receptor, and a second receptor, ErbB1, which have been implicated in the growth of various tumour types. Stimulation of ErbB1 and ErbB2 is associated with cell proliferation, and with multiple processes involved in tumour progression, invasion and metastasis.

Current information suggests that lapatinib will be used in combination with letrozole for first line treatment of women with previously untreated advanced breast cancer.

Intervention(s)	Lapatinib (in combination with letrozole)
Population(s)	Post menopausal women with previously untreated advanced or metastatic breast cancer which is oestrogen receptor and/or progesterone receptor positive
Standard comparators	<ul style="list-style-type: none"> • Hormone manipulation, without lapatinib
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression free survival • response rate • adverse effects of treatment • health-related quality of life.

¹ Immunohistochemical techniques can detect the amount of HER2 protein in a tumour sample. The HER2 level is graded from 0 to 3+. A grade 3+ means that there is a higher than normal level of HER2 protein (over-expression) and the result is considered HER2-positive. However, this technique is not as definitive as molecular techniques such as FISH (Fluorescence in situ hybridisation) which can detect excessive amounts (amplification) in each cell of the HER2/neu gene, which leads to the over-production of the HER2 receptor protein.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The time horizon of the analysis should attempt to capture the benefits/costs over the period during which the effects of the treatment may be expected to differ from the comparator.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
<p>Other considerations</p>	<p>The intervention will be appraised according to its/their anticipated marketing authorisation. Guidance will only be issued in accordance with the Summary of Product Characteristics.</p>

<p>Related NICE recommendations</p>	<p>Related Technology Appraisals:</p> <ul style="list-style-type: none"> • Capecitabine for the treatment of locally advanced or metastatic breast cancer (2003) • Trastuzumab for advanced breast cancer (2002) • Vinorelbine for advanced breast cancer (2002) • Taxanes for the treatment of breast cancer (2001) <p><i>Appraisals in progress</i></p> <ul style="list-style-type: none"> • Hormonal therapies for the adjuvant treatment of early oestrogen-receptor positive breast cancer (Multiple Technology Appraisal) • Docetaxel for the treatment of early breast cancer (Single Technology Appraisal) • Paclitaxel for the treatment of early breast cancer (Single Technology Appraisal) • Trastuzumab as adjuvant therapy for early breast cancer (Single Technology Appraisal) • Gemcitabine for the treatment of locally advanced or metastatic breast cancer (Single Technology Appraisal) <p>Cancer service guidance:</p> <ul style="list-style-type: none"> • Improving outcomes in breast cancer (2002) <p>Related Guidelines:</p> <ul style="list-style-type: none"> • Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (2004, CG014) <p><i>Guidelines in progress</i></p> <ul style="list-style-type: none"> • NICE clinical guideline on the diagnosis and treatment of breast cancer (9th wave) • Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (partial update of CG014)
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Questions for consultation

It is anticipated that this technology will be appraised through the Single Technology Appraisal (STA) process. Are there any reasons why this may not be appropriate? Note that there will be another STA to consider an additional indication in breast cancer.

Which hormonal treatments should be included as comparators? Should lapatinib plus letrozole be compared with letrozole alone, or are other hormonal treatments also appropriate for inclusion as comparators?

Would chemotherapy be an appropriate comparator? If so, which regimens?

Is the population appropriately defined? Should only women with tumours that over-express HER2 be included?

What is the definition of 'locally advanced in terms of staging based on tumour, nodes and metastases?